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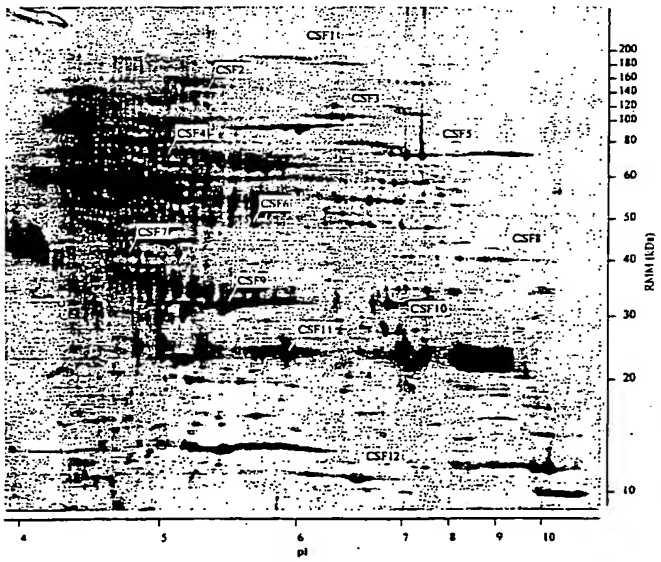
[Continued on next page]

(54) Title: PROTEINS, GENES AND THEIR USE FOR DIAGNOSIS AND TREATMENT OF VASCULAR DEMENTIA



(57) Abstract: The present invention provides methods and compositions for screening, diagnosis and prognosis of Vascular Dementia, for monitoring the effectiveness of Vascular Dementia treatment, identifying patients most likely to respond to a particular therapeutic treatment and for drug development. Vascular Dementia-Associated Features (VFs), detectable by two-dimensional electrophoresis of cerebrospinal fluid, serum or plasma are described. The invention further provides Vascular Dementia-Associated Protein Isoforms (VPIs) detectable in cerebrospinal fluid, serum or plasma, preparations comprising isolated VPIs, antibodies immunospecific for VPIs, and kits comprising the aforesaid.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/01106

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/68 C07K14/47 A61P9/10 A61P25/28 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS, EMBL, WPI Data, PAJ, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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A	abstract page 193, left-hand column, line 3 -right-hand column, line 3 page 194, right-hand column, paragraph 2 page 195, left-hand column, paragraph 5 -page 196, paragraph 3	6,7

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
8 January 2002	23. 01. 2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gundlach, B

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropnate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/01106

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LITTLE S P ET AL: "ZYME, A NOVEL AND POTENTIALLY AMYLOIDOGENIC ENZYME CDNA ISOLATED FROM ALZHEIMER'S DISEASE BRAIN" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 272, no. 40, 1997, pages 25135-25142, XP002926885 ISSN: 0021-9258 abstract -& DATABASE SWISS-PROT 'Online! ID: KLK6_HUMAN AC: Q92876, XP002186528 cited in the application abstract ---	8-46
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/01106

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 01/01106

Box I Observations where certain claims were found unsearchable (Continuation f it m 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: –
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210 .

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

All claims relating to (VF-4) VPI-2, VPI-29, VPI-15, VPI-21, VPI-273 and VPI-154

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 24, 25, or 26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: Claims 1-7 (partially)

   Diagnosis of vascular dementia using VF-4 as marker.

2. Claims: Inventions 2-712: Claims 1-46 (all partially)

   Diagnosis or treatment of vascular dementia using one of VF-5 to VF-372 or one of VPI-2 to VPI-273 as marker/target.

3. Claims: Invention 713: 47-54 (fully)

   Method of screening for agents effective for the treatment of vascular dementia involving IGF-II

4. Claims: Invention 714: Claims 55-62 (fully)

   Method of screening for agents effective for the treatment of vascular dementia involving TIMP-1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 01/01106

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